

An Adolescent With Nonsuicidal Self-Injury: A Case and Discussion of Neurobiological Research on Emotion Regulation

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The management of nonsuicidal self-injurious behavior is a common focus of clinical care, particularly in the treatment of adolescents and young adults. Increased recognition of this problem has led to proposed criteria for future study in DSM-5, which may be beneficial in advancing the field. Clinical care may be fruitfully informed by an understanding of the neurodevelopmental underpinnings of this behavior. The authors discuss the current status of neurobiological research related to nonsuicidal self-injury with a focus on the key dimension of emotion regulation. A case is presented to illustrate the critical points. Preliminary empirical evidence suggests disturbances in neurobiological systems relevant to emotion

regulation. Disturbances involve engagement of limbic brain regions and frontal regulatory brain regions that may evolve over time. Additionally, disturbances are observed in serotonin and physiological response systems relevant to emotion regulation. Treatment with serotonin reuptake inhibitors may be most beneficial in combination with dialectical behavioral therapy to address safety, build self-soothing strategies to enhance emotion regulation, and reduce interpersonal sensitivity. Delineation of the neurobiological markers that reflect successful treatment response will help in the identification of new avenues for research and the development of personalized treatments for adolescents with nonsuicidal self-injury.

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Nonsuicidal self-injury is the act of harming one's own body tissue without the intent to die (1). Onset is typically in adolescence or early adulthood, and the average prevalence in adolescents around the world is 18% (2). Increased recognition of this problem has led to proposed criteria for future study in DSM-5. Although commonly associated with a wide range of clinical problems such as depressive, borderline personality, anxiety, substance abuse, eating, and developmental disorders, some adolescents with nonsuicidal self-injury do not meet criteria for any psychiatric disorders (3). For example, Veronica, in the case vignette, had a history of depression but did not meet criteria for any axis I or II disorders, either at the onset of nonsuicidal self-injury or at the time of our evaluation.

Adolescence is a period notable for substantial emotional and behavioral challenges that correspond with important brain developmental changes. When adolescents experience strong negative emotions, they experiment with a range of coping behaviors, some of which may be maladaptive, such as substance use, disordered eating patterns, and nonsuicidal self-injury. For example, after an initial social exposure, Veronica experimented with nonsuicidal self-injury and it quickly became her primary tool for regulating negative affect. What biological mechanisms predisposed her to initiate, incorporate, and maintain nonsuicidal self-injury? Consideration of this question should

ideally take into account the complex interplay in which environment, genes, and behavior contribute to shape neurodevelopmental trajectories. In keeping with the National Institute of Mental Health's Research Domain Criteria initiative (4), one approach is to examine key psychological dimensions of functioning that relate to nonsuicidal self-injury and to neurobiology. Candidate dimensions include emotion regulation, social processes, pain, reward, and others. In this discussion, we focus on emotion regulation, which, as Veronica's case illustrates, directly relates to the onset and maintenance of nonsuicidal self-injury.

Emotion Regulation in Nonsuicidal Self-Injury

A disturbance in emotion regulation is a primary characteristic of individuals with nonsuicidal self-injury (5). Like Veronica, such individuals usually perform self-injury with the purpose of relieving negative affect (6). Current developmental theory holds that emotion dysregulation fosters and maintains nonsuicidal self-injury in hostile and invalidating social contexts (7). Consistent with research showing that parental antipathy and criticism are important factors in the development of nonsuicidal self-injury (8, 9), Veronica's early upbringing was characterized by periods when her parents were more aggressive and less emotionally nurturing. In Veronica's

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“Veronica” is a 15-year-old Caucasian girl who presented as a volunteer for a study of nonsuicidal self-injury. Veronica began cutting herself at age 13 in seventh grade after learning about this behavior from friends. After trying it once or twice, she said, she “was hooked.” Initially she cut herself on her forearms, but then switched to her upper thighs to conceal the injuries. Veronica’s primary reason for engaging in self-injury was to release built-up emotional pressure. Episodes typically occurred after an emotional conflict with her parents or a perceived rejection by a peer. The frequency of self-injury episodes ebbed and flowed, ranging from daily to monthly.

The diagnostic evaluation revealed that for Veronica, depressive symptoms began insidiously during middle school, and rose to meet criteria for a moderately severe episode of major depression when she was in eighth grade. Around that time, Veronica’s parents sought a mental health evaluation for her, where it was recommended that she begin weekly supportive counseling. However, Veronica did not feel “connected” to her therapist and attended only a few sessions. Her parents then brought her to their family physician, who prescribed fluoxetine. Veronica and her parents agreed that the medication led to a significant improvement in her overall depressive symptoms. However, she continued to engage in self-injury about twice a month.

Veronica’s medical and early developmental history was unremarkable. Her family history was notable for a history of depression for her mother and a history of alcoholism (with 3 recent years of sobriety) for her father. Her social history was notable for environmental stressors throughout childhood. Veronica’s parents described periods during her early childhood when the household was chaotic, characterized by shouting and occasional physical altercations between the parents or toward the children. There was no clear history of child abuse or neglect. Veronica’s parents divorced when she was in the fifth grade; since then, they have had joint custody of Veronica and her two siblings. Conflict between parents persisted

even after the divorce. Additionally, Veronica described her older brother as being “mentally abusive” toward her, and reported that she argued almost constantly with her younger sister. Veronica’s history of peer relationships was characterized by instability and uncertainty, marked by occasional turmoil, which she referred to as “drama.” Veronica is now in the tenth grade at a large high school, where she has maintained a B average and currently has a moderately sized peer group consisting of relatively recent friendships.

Physical examination revealed an average height and weight and was notable only for scarring and some recent self-inflicted superficial wounds on her arms and legs. Veronica was pleasant and cooperative, forthcoming and direct in her communication style. She denied current suicidal thoughts. Results from a battery of self-report psychological assessments indicated only a mild level of depressive symptoms but significantly elevated levels of alexithymia, egocentrism, hostility, and interpersonal sensitivity. Several disturbances in emotion regulation were noted, including nonacceptance of emotional responses, lack of emotional awareness, and limited access to emotion regulation strategies.

Veronica was referred to the child and adolescent psychiatry clinic at the University of Minnesota. She was continued on fluoxetine and began participating in weekly individual, family, and group sessions in the dialectical behavioral therapy program. The initial focus of therapy was to address safety concerns. Nonsuicidal self-injury declined substantially within the first month of treatment, and ceased 2 months later. Veronica made significant gains in her ability to identify her emotions and to tolerate emotional distress. She utilized a variety of techniques to reach these goals and found that self-soothing strategies were particularly effective for regulating her emotions. Her interpersonal relationships matured, with an improvement in perspective-taking and an accompanying decrease in interpersonal sensitivity and hostility. However, family conflict persisted, so a referral was made for family therapy.

assessment, she exhibited deficits in emotion understanding and coping strategies, both dimensions that are ideally fostered in the setting of a supportive home environment with positive parental modeling. In this setting, the neural substrates for these dimensions of emotion regulation may have developed aberrantly, predisposing her to develop and maintain nonsuicidal self-injury.

Biological Mechanisms in Emotion Regulation and Nonsuicidal Self-Injury

Research in several branches of affective neuroscience has shown early progress in understanding how biological substrates of emotion regulation may be awry in youths with nonsuicidal self-injury. Clinical care may be fruitfully informed by an understanding of the neurodevelopmental underpinnings of this behavior. Here we briefly review

recent research that uses diverse methodologies to measure neurobiological aspects relevant to emotion regulation in nonsuicidal self-injury, including 1) neural circuitry implicated in emotion processing, 2) the serotonin system, and 3) the functioning of the physiological stress response system, including the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis.

Neuroimaging studies have begun to examine the neural underpinnings of emotion regulation in nonsuicidal self-injury. Studies of adults with borderline personality disorder who also have nonsuicidal self-injury have found enhanced amygdala activation to negative and neutral faces (which was positively correlated with self-reported affective dysregulation) (10). Other work has shown that relative to a healthy comparison group, adults with borderline personality disorder and nonsuicidal

self-injury showed diminished activation of the orbitofrontal and midcingulate cortex but enhanced activation of the dorsolateral prefrontal cortex while listening to a script describing the stages of an act of nonsuicidal self-injury (11). Interestingly, these findings only partly agree with the one published study of adolescents with nonsuicidal self-injury. Relative to comparison subjects, adolescents with nonsuicidal self-injury (N=9) showed enhanced limbic activity in response to emotional pictures, as well as enhanced orbitofrontal, inferior, and middle frontal cortex activity while viewing nonsuicidal self-injury-related pictures (12). The divergent pattern of cortical responses across studies could stem from methodological differences (i.e., different inclusion criteria [nonsuicidal self-injury versus borderline personality disorder], different functional MRI paradigms), or it could reflect a developmental difference. Perhaps in cases like that of Veronica, limbic hyperactivity to threat stimuli remains a chronic trait, whereas across the transition to adulthood, orbitofrontal hyperactivity shifts to hypoactivity. Such a shift could result from processes related to neurodevelopment, chronicity, or accommodation. Clearly, this early cross-sectional work needs replication and expansion, and longitudinal studies are needed to test hypotheses about how differences unfold over time.

The serotonin system, which plays a key role in mood and is relevant to emotion regulation, has been examined in nonsuicidal self-injury research (1). Serotonin has been implicated in suicide and related behaviors (13). Reduced 5-HT₂ binding in the frontal cortex has been documented in unmedicated adults with nonsuicidal self-injury (14). Lower CSF levels of serotonin metabolites have been found in patients with both major depression and nonsuicidal self-injury compared with major depression without nonsuicidal self-injury (15). Although the serotonin transporter gene (5HTTLPR) has been associated with suicidal behavior (16), a recent study in women with borderline personality disorder found that this polymorphism was associated with other borderline symptoms but not with nonsuicidal self-injury (17). Despite the relative success in using serotonergic medications for related conditions such as depression and anxiety, a recent review suggested limited success in trials that have focused on nonsuicidal self-injury (18). This is consistent with Veronica's case, in which self-injury persisted despite an improvement in depressive symptoms in response to fluoxetine.

Research on nonsuicidal self-injury has begun to investigate physiological systems implicated in emotion regulation, such as the autonomic nervous system and

HPA systems. Studies focusing on the autonomic nervous system have utilized methods assessing the defensive startle reflex, electrodermal response, and heart rate variability. Studies of heart rate variability (19) and defensive startle reflex (20) have failed to differentiate adolescents with nonsuicidal self-injury from healthy subjects, despite elevated subjective emotional responses in the nonsuicidal self-injury group (20). Electrodermal response studies in adolescents with nonsuicidal self-injury have documented attenuated response during resting conditions (21) but elevated response during frustration (22). In an HPA study, adolescents with nonsuicidal self-injury showed attenuated cortisol response

to a social challenge despite self-reported emotional response comparable to healthy subjects (19). Tentatively, these findings may indicate a pattern of underresponding rather than overresponding, potentially suggesting an allostatic shift in physiological systems to accommodate chronic stress. For example, the chronic stress of Veronica's chaotic developmental environment may have resulted in blunting of physiological responses to stress, despite ongoing emotional responses to evocative situations (which she referred to as "drama.")

These hypotheses need further testing in youths with nonsuicidal self-injury, and they raise the question of whether treatment could reverse these shifts to normalize physiological responses.

Treatment

Although no validated treatments are currently available that specifically target adolescents with nonsuicidal self-injury, some approaches have been used clinically and are under investigation with this population. For example, dialectical behavioral therapy is directed toward addressing affective instability associated with nonsuicidal self-injury, and it has shown early promising results in adolescents with nonsuicidal self-injury (23). Mentalization-based treatment has also been investigated and shown promise for this group (24).

Summary and Future Directions

A greater understanding of the neurobiology of nonsuicidal self-injury will enhance our ability to treat our patients. Research on nonsuicidal self-injury is still in its infancy, especially regarding adolescents. A promising research approach is to focus on dimensions of functioning (rather than categorical illnesses) that relate to nonsuicidal self-injury and map onto neurobiology. In this article, we have focused on the dimension of emotion regulation. Preliminary evidence suggests that emotion

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regulation disturbances related to nonsuicidal self-injury involve strong engagement of limbic brain regions but that abnormalities in engagement of frontal regulatory regions may change over time as a result of neurodevelopment, chronicity, or accommodation. Research on serotonin systems has shed some light on self-injury behaviors but has not yet led to clear treatment solutions. Results on the functioning of physiological response systems suggest that diminished rather than elevated arousal of some key systems may reflect allostatic shifts taking place. Longitudinal studies are needed to tease apart which biological abnormalities represent predisposing factors, which only emerge concurrently with initiation of nonsuicidal self-injury, and how the systems change with chronicity.

The most promising next steps for research include neurobiological studies in the context of treatment interventions. For example, many of Veronica's symptoms improved with dialectical behavioral therapy; characterization of the changes that accompany such treatment response will provide important new insights into the pathophysiology of this behavior. Furthermore, delineation of the neurobiological markers that distinguish patients who do not respond to various treatments will help in the identification of new avenues for research and the development of personalized treatments for adolescents with nonsuicidal self-injury.

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